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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/361,652	07/27/1999	CHARLES S. ZUKER	2307E-88610	5785

20350 7590 09/09/2008

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1649	

MAIL DATE	DELIVERY MODE
09/09/2008	PAPER

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte
CHARLES S. ZUKER, JON E. ADLER, JUERGEN LINDEMEIER, NICK RYBA, and MARK HOON

Appeal 2008-2934
Application 09/361,652
Technology Center 1600

Decided: September 9, 2008

Before TONI R. SCHEINER, DONALD E. ADAMS, and ERIC GRIMES, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to nucleic acid encoding a G-protein coupled receptor. The claims have been finally rejected as lacking utility, and lacking enablement. We have jurisdiction under 35 U.S.C. § 6(b).

BACKGROUND

"Taste transduction is one of the most sophisticated forms of chemotransduction in animals . . . ; its main purpose is to provide a reliable signaling response to non-volatile ligands" (Spec. 1: 24-29). "Mammals are believed to have five basic taste modalities: sweet, bitter, sour, salty and unami (the taste of monosodium glutamate)" (Spec. 2: 1-2).

"Each of these modalities is though[t] to be mediated by distinct signaling pathways mediated by receptors or channels, leading to receptor cell depolarization, generation of a receptor or action potential, and release of neurotransmitter at gustatory afferent neuron synapses" (Spec. 1: 29-32). "Sweet, bitter, and unami transduction are believed to be mediated by G-protein-coupled receptor (GPCR) signaling pathways" (Spec. 3: 7-8). "However, little is known about the specific membrane receptors involved in taste transduction, or many of the individual intracellular signaling molecules activated by the individual taste transduction pathways" (Spec. 3: 14-16).

In mammals, taste receptor cells are assembled into taste buds that are distributed into different papillae in the tongue epithelium. Circumvallate papillae, at the very back of the tongue, are particularly sensitive to bitter substances. Foliate papillae, located on the posterior lateral edge of the tongue, are particularly sensitive to sour and bitter substances. Fungiform papillae, at the front of the tongue, are thought to mediate much of the sweet taste modality. (Spec. 2: 14-21.)

The present invention is directed to nucleic acid encoding rat GPCR-B3, a taste cell specific G-protein-coupled receptor (Spec. 3: 31-33), and its

murine and human homologs. Rat GPCR-B3 was originally isolated as a "moderately rare sequence . . . from an oligo-dT primed circumvallate cDNA library" (Spec. 10: 8-10), and is also "specifically expressed in foliate and fungiform cells" (Spec. 10: 7-8).

STATEMENT OF THE CASE

Claims 1, 4-6, 8, 34, 35, and 61-67 stand rejected under 35 U.S.C. § 101 as lacking utility. In addition, claims 1, 4-6, 8, 34, 35, and 61-67 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement.[1]

Claims 1 and 61 are representative of the claimed subject matter:

1. An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the receptor comprises an amino acid sequence having at least 80% identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds to glutamate, which induces GPCR activity.

61. A method of making a taste transduction G-protein coupled receptor, the method comprising the step of expressing the receptor from a recombinant expression vector comprising a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds glutamate, which induces GPCR activity.

SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 represent the predicted amino acid sequences of the rat, mouse and human GPCR-B3s, respectively (Spec. 59: 1 to 60: 15).

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[1] A rejection of the claims under 35 U.S.C. § 112, first paragraph, as lacking adequate written descriptive support was withdrawn by the Examiner (Ans. 2).

DISCUSSION

The Examiner rejected claims 1, 4-6, 8, 34, 35, and 61-67 under 35 U.S.C. § 101 "because they are drawn to an invention with no apparent or disclosed **specific** and substantial credible utility in currently available form" (Ans. 3).

Appellants contend that the Specification teaches that GPCR-B3 is "a GPCR expressed specifically in taste cells . . . [and] is a component of the taste signal transduction pathway and is capable of, via its interaction with a G-protein, mediating taste (such as sweet, bitter, unami, *etc.*) perception" (App. Br. 7). It is asserted that "probes for GPCR polypeptides and proteins can be used to identify subsets of taste cells such as foliate cells and circumvallate cells, or specific taste receptor cells, e.g., sweet, sour, salty, and bitter . . . , to dissect taste-induced behaviors" and "to identify high affinity agonists and antagonists of taste cell activity . . . [which] can then be used in the food and pharmaceutical industries to customize taste" (Spec. 8: 21 to 9: 1).

The Examiner does not dispute that GPCR-B3 "is a [G] protein-coupled receptor that is expressed specifically in taste cells" (Ans. 4), but argues that there is no evidence that GPCR-B3 is actually involved in taste perception (*id.* at 7). The Examiner contends that "a method of 'identifying a compound that **modulates sensory signaling** in sensory cells' is not a specific utility and that additional experimentation is required before a practical utility . . . can be established" (*id.* at 3).

The issue raised by this appeal, then, is whether any utility asserted by Appellants satisfies the requirement for a substantial and specific utility, in currently available form. The following facts are relevant to this issue:

FF1. According to the Specification, "'[t]aste receptor cells' are neuroepithelial cells that are organized into groups to form taste buds of the tongue, e.g., foliate, fungiform, and circumvallate cells" (Spec. 11: 29-30).

FF2. The Specification teaches that foliate papillae, located on the posterior lateral edge of the tongue, are particularly sensitive to sour and bitter substances. Fungiform papillae, at the front of the tongue, are thought to mediate much of the sweet taste modality. Circumvallate papillae, at the very back of the tongue, are particularly sensitive to bitter substances. (Spec. 2: 14-21.)

FF3. The Specification states that "[s]weet, bitter, and unami transduction are believed to be mediated by G-protein-coupled receptor (GPCR) signaling pathways. . . . However, little is known about the specific membrane receptors involved in taste transduction" (Spec. 3: 7-15).

FF4. According to the Specification, "sensory GPCRs have an N-terminal 'extracellular domain,' a 'transmembrane domain' comprising seven transmembrane regions and corresponding cytoplasmic and extracellular loops, and a C-terminal 'cytoplasmic domain'" (Spec. 12: 23-25). The extracellular domain protrudes from the cellular membrane and binds to extracellular ligand (Spec. 12: 31-32).

FF5. The Specification states that cDNA encoding rat GPCR-B3 (SEQ ID NO:1) was isolated as a "moderately rare" sequence from a rat circumvallate papillae library, and is also expressed in foliate and fungiform

papillae. (Spec. 10: 7-10, 56: 1-15.) SEQ ID NO:2 and SEQ ID NO:3 represent the mouse and human homologs, respectively. The human homolog was isolated from a testis library (Spec. 10: 1-7, 57: 13-28).

FF6. According to the Specification, "[t]hese taste cell specific GPCRs are components of the taste transduction pathway" (Spec. 4: 1-2).

FF7. Figure 4 of the Specification is a graphic representation of a chimeric receptor "containing the entire extracellular domain of the murine mGluR1 receptor and the transmembrane domain comprising seven transmembrane regions and corresponding cytosolic loops, and C-terminal end from murine GPCR-B3" (Spec. 8: 4-7).

FF8. Figure 5 of the Specification "shows HEK cells transfected with the chimeric glutamate/GPCR-B3 receptor described in Figure 4", and stimulated with glutamate, the mGluR1 ligand (Spec. 8: 8-9). As explained by Dr. Charles Zuker, in his declaration dated September 10, 2002, the transfected cells "demonstrated an increase in intracellular calcium in response to the ligand, indicating that the chimeric GPCR couples to a promiscuous G protein and triggers calcium responses" (Dec. ¶ 9). Dr. Zuker further explains that these data demonstrate "that GPCR-B3 is a functional G-protein coupled receptor" (*id.*), and contends that "one of skill in the art, at the time the application was filed, would immediately recognize the real world utility of the nucleic acids of this invention" (Dec. ¶ 11).

FF9. It is asserted that in the Specification that "probes for GPCR polypeptides and proteins can be used to identify subsets of taste cells . . . or specific taste receptor cells, e.g., sweet, sour, salty, and bitter . . . , to dissect taste-induced behaviors" and "to identify high affinity agonists and

antagonists of taste cell activity . . . [which] can be used in the food and pharmaceutical industries to customize taste" (Spec. 8: 21 to 9: 1).

FF10. The Specification does not disclose a ligand for any of the GPCR-B3s encoded by the claimed nucleic acids, or a specific signal transduction pathway activated by the GPCR-B3s.

FF11. According to Nelson et al.,[2] a reference published after the filing date of the instant application, mouse T1R1 (the same protein as the instant mouse GPCR-B3) and T1R3 (a component of T1R2+3, a sweet taste receptor), were expressed in HEK cells

> alone or in combination and tested for stimulation by L-amino acids. Individual receptors showed no responses. In contrast, T1R1 and T1R3 combine to function as a broadly tuned L-amino acid receptor, with most amino acids that are perceived as sweet (for example, alanine, glutamine, serine, threonine and glycine) activating T1R1+3 . . . The responses are strictly dependent on the combined presence of T1R1 and T1R3 . . .

(Nelson 1, paragraph bridging cols. 1 and 2, internal citation omitted). Based on their experimental data, Nelson et al. "propose that T1R1+3 is a constituent of the umami response" (Nelson 3, col. 1).

DECISION

Given these factual findings, we agree with the Examiner that the Specification does not disclose a utility for GPCR-B3 that satisfies 35 U.S.C. § 101. As noted by the Examiner, § 101 requires a utility that is both substantial and specific. *In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir. 2005).

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[2] Nelson et al. ("An Amino-Acid Taste Receptor," *Nature* advance online publication, 24 February 2002 (DO1 10.1038/nature726)).

A substantial utility is one that "show[s] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." *Id.* A specific utility is one "which is not so vague as to be meaningless." *Id.* In other words, "in addition to providing a 'substantial' utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public." *Id.*

Appellants contend that GPCR-B3 is "expressed specifically in taste cells" and "[i]t is asserted in the specification that . . . [GPCR-B3] is a component of the taste signal transduction pathway . . . [that] is capable of, via its interaction with a G-protein, mediating taste (such as sweet, bitter, unami, *etc.*) perception" (App. Br. 7). "It is further asserted that GPCR-B3 polypeptides or the encoding nucleic acids can be used, for example, as probes to identify taste cells, to generate taste topographic map[s], and to provide a screening method for compounds that can modulate taste signaling and are therefore useful in the food and pharmaceutical industries" (*id.*).

As discussed above, there is no dispute that GPCR-B3s are G protein-coupled receptors expressed by taste receptor cells in circumvallate, foliate, and fungiform papillae (FF 1-3, 5, 8, Ans. 4). Nevertheless, although the instant Specification suggests that GPCR-B3s "are components of the taste transduction pathway" (Spec. 4: 1-2; FF6), it does not disclose GPCR-B3's role in modulating any of the basic taste modalities, much less which one(s)

(FF10). Nor does the Specification disclose any ligands that bind the extracellular domain of GPCR-B3 (FF10).

We agree with the Examiner that "a method of 'identifying a compound that modulates sensory signaling in sensory cells'" (Ans. 3, emphasis omitted), without a more precise identification of the modulated signal, does not provide a substantial or specific, currently available benefit to the public. Nor are we persuaded by the assertion that GPCR-B3 can be used to identify specific taste receptor cells (e.g., sweet, sour, salty, and bitter), or "subsets" of taste cells (Spec. 8: 21-24), since it is expressed in the three types of papillae that contain taste receptor cells: circumvallate, foliate, and fungiform (FF9).

Moreover, it was determined after the filing date that a heterodimer of GPCR-B3 (T1R1) and T1R3 functions as a broadly tuned L-amino acid receptor, but GPCR-B3, on its own, is unresponsive to any of the ligands tested, including glutamate (Nelson 1, FF 11). In addition, the Specification does not disclose that GPCR-B3 is an L-amino acid receptor, nor does the evidence of record show that it was known to be an L-amino acid receptor at the time the instant application was filed. Utility is determined as of the filing date. *In re Brana*, 51 F.3d 1560, 1567 n.19 (Fed. Cir. 1995).

Appellants contend that "[t]he Nelson *et al.* reference was provided merely as an example of confirmed involvement of GPCR-B3 in taste signaling" and "to demonstrate the credibility of the asserted utility that GPCR-B3 is involved in taste signaling and is therefore useful in, *e.g.*, screening methods for identifying taste-modulating compounds" (App. Br. 8). "[W]hether or not the specification describes this particular heterodimer

of GPCR-B3 and T1R3 is not directly relevant to whether one of skill in the art would find the asserted utility credible" and in any case, the credibility of the asserted utility "has already been established by Dr. Zuker's declaration" (*id.* at 8-9). Appellants add that "it is possible that GPCR-B3 can act alone or in complex with other proteins . . . to mediate taste signal transduction" (*id.*).

This argument is not persuasive. The issue is not whether the assertion that GPCR-B3 is "involved" in taste signaling is credible. The issue is whether the Specification's disclosure (together with what was known in the art as of the filing date) is sufficiently detailed to provide a substantial and specific, currently available benefit to the public. We agree with the Examiner that it does not.

We therefore affirm the rejection of the claims under 35 U.S.C. § 101 based on lack of utility.

Enablement

The Examiner also rejected claims 1, 4-6, 8, 34, 35, and 61-67 under 35 U.S.C. § 112, first paragraph, "as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101" (Ans. 11).

This rejection is a corollary of the utility rejection, and is affirmed for the same reasons.

SUMMARY

The rejections of claims 1, 4-6, 8, 34, 35, and 61-67 under 35 U.S.C. §§ 101 and 112, first paragraph, are affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv) (2006).

AFFIRMED

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